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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/362,485	07/28/99	FLOHE L	29473/35834

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EXAMINER	
JOHANNSEN, D	
ART UNIT	**PAPER NUMBER**
1655	11

DATE MAILED: 07/17/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/362,485	Flohe et al
Examiner	**Group Art Unit**
Diana Johannsen	1655

☒ Responsive to communication(s) filed on *May 26, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-8 and 10-18* is/are pending in the application.

Of the above, claim(s) *2-8 and 10-18* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This application is a continuation of international application PCT/EP98/00483, filed January 29, 1998.

Election/Restriction

2. Applicant's election with traverse of claim 1 in Paper No.10 is acknowledged.

With respect to restriction between Groups I and II, the traversal is on the ground(s) that "no example has been cited using the combined components of the invention in a manner different from the processes as claimed". However, Group I is drawn not to a method, but to a collection of products. While claim 1 sets forth an intended use for the claimed products ("for the diagnosis of tuberculosis and other mycobacterial infections..."; "for the determination of the activity of alanine dehydrogenase"), the intended use of a product for which a clear and complete structural description is provided is not accorded patentable weight (see MPEP 2111.02). Accordingly, Group I encompasses merely a "set" of products, without limiting the manner in which those products may be used. Furthermore, in light of Applicant's amendment of claim 1 to include "a DNA sequence", Groups I and II are no longer related as product and process of use, as set forth in the Office action of paper no. 9. While the products in the "enzymatic test kit" of claim 1 are disclosed as capable of use in the methods of Group II, the "set" of amended claim 1 (which includes a DNA sequence) is not. Accordingly, Invention I and Invention II are now unrelated, as they are not disclosed as capable of use together (MPEP § 806.04, MPEP § 808.01).

With respect to restriction between Groups I and III, the traversal is on the ground(s) that the inventions of Groups I and Group III are disclosed as capable of use together. The traversal cites page 4, lines 19-22, page 2, lines 22-27, page 5, lines 12-25, and page 37, lines 5-7 of the specification in support of this assertion. Page 2, lines 22-27 of the specification set forth an "enzymatic test kit" and the components thereof which may be used for diagnosis of tuberculosis and other mycobacterial infections. Page 4, lines 19-22 of the specification indicates that DNA sequence from the alanine dehydrogenase gene of *M. tuberculosis* may be used for diagnosis of tuberculosis and other mycobacterial infections, and page 5, lines 12-25 describes a DNA-based detection method that comprises steps of restriction digestion and amplification. Page 37, lines 5-7 of the specification states that "The disclosure also includes all conceivable combinations of the individual features disclosed". However, the specification does not actually disclose a method in which both the "enzymatic test kit" and the "DNA sequence" set forth in claim 1 are employed. Absent an actual disclosure in the originally filed specification of a "set" comprising the components set forth in amended claim 1 and/or of a method in which all of this components are employed, it cannot be said that the specification actually discloses the use together of the inventions of Groups I and III. Further, Group III is directed to methods in which only the use of the "DNA sequence of claim 1" is required; thus, it appears that the invention as claimed does not require the "enzymatic test kit" of claim 1, or the "set" of claim 1. Accordingly, Inventions I and III are properly considered to be unrelated inventions.

The traversal further argues that "the restriction requirement is improper because it does not meet the requirement that search and examination of the entire application must be a serious burden on the examiner", and that "a complete search directed to the subject matter of the claims of Group II or the claims of Group III would require a search direct to the subject matter of the claims of Group I, and vice versa". However, in actuality, the search terms and strategies used to identify art relevant to the products of Group I and the methods of Groups II and III differ from one another. Specifically, a search of Group I as claimed requires identification of art relevant to the products claimed, and does not require search and identification of the particular methods of either Group II or Group III. Similarly, while each of Groups II and III would require search and identification of methods in which some of the components of the "set" of claim 1 would be employed, the methods as claimed do not require the "set" of claim 1. While the traversal asserts that claim 1 is a linking claim that links the dependent claims of Groups II and Group III, neither the claims of Group II nor the claims of Group III properly depend from claim 1, as the claimed methods do not incorporate all the limitations of claim 1 (specifically, Group II requires only "an enzymatic test kit according to claim 1", while Group III requires only "said DNA sequence of claim 1"). Furthermore, the three inventions are classified differently and have acquired separate status in the art.

Accordingly, because Inventions I-III are distinct from one another for the reasons given above and have acquired a separate status in the art as demonstrated by their different classifications and recognized divergent subject matter, and because a search of each of the three

Inventions would require different searches and identification of different art, examination of these distinct inventions would pose a serious burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Specification

3. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(i) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing (see 37 CFR 1.821-1.825).

The specification should be amended in accordance with the above guidelines. It is particularly noted that Applicant has not provided a "Brief Description of the Figures", as required by 37 CFR 1.74 (*see MPEP 608.01(f)*).

4. The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a) and (a)(2). However, the specification fails to comply with one or more of the requirements of 37 CFR § 1.821 through 1.825 because the claims and specification recite sequences that lack description by the appropriate sequence identifiers set forth in the "Sequence Listing" as required by 37 CFR § 1.821(d). See, for example, claim 1 and pages 4, 14, and 31. Furthermore, the Description of the Figures (see paragraph 3, above) must set forth the sequence identifiers of any sequences recited in the figures (see MPEP 2422.02). Appropriate corrections for compliance are required.

It is further noted that the nucleotide sequence of the primer "AlaDH-F2" set forth on page 4 and in claim 1 differs from that set forth in Table 2.5 (page 14) and described as "SEQ ID NO: 13". The specification must be amended such that it accurately sets forth the sequence of "AlaDH-F2" throughout the specification, claims, and Sequence Listing. **If necessary (i.e., if the sequence set forth as SEQ ID NO: 13 is incorrect), Applicant must comply with the requirements of 37 CFR 1.821 through 1.825** as set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant is requested to return a copy of the attached Notice to Comply with the response to this Office action.

Information Disclosure Statement

5. It is noted that the Examiner has provided complete citations for the Kannan et al and Andersen et al references set forth on the PTO-1449 submitted by Applicant on October 29, 1999 (paper no. 7).

Claim Rejections - 35 U.S.C. § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is drawn to a "set" comprising an "enzymatic test kit" and a DNA sequence. However, while the specification as originally filed teaches both the enzymatic test kit and the DNA sequences set forth in the claims, the specification does not disclose a "set" as required by the claim. Further, the specification does not disclose any product or composition comprising such components that could be considered to constitute a "set", or disclose, e.g., a method in which such a combination of components is employed. Accordingly, the specification does not provide basis for the "set" of claim 1.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite over the recitation of the phrase "set...comprising....an enzymatic test kit....and...a DNA sequence". A definition for the term "set" as it pertains to the invention is not provided in the specification, and it is unclear as to what is meant and encompassed by this language. For example, must a "set" comprising an enzymatic test kit and a DNA sequence have a particular structural form, or is this language sufficiently broad so as to encompass the mental concept of a "set"? The claim should be amended so as to provide a clear description of the structural and functional properties of the product encompassed thereby.

Claim 1 is indefinite over the recitation of the terms "DNA sequence" and "sequences". It is unclear as to whether this language is intended to refer to, e.g., a DNA molecule or fragment thereof, or whether Applicant intends for the claim to encompass, e.g., the mere recitation of a particular sequence of nucleotides (as opposed to, e.g., a molecule consisting of or comprising that sequence). Clarification is required.

Claim 1 is indefinite over the recitation of the phrase "the following partial sequences and other partial sequences of the alanine dehydrogenase gene of *M. tuberculosis* (Fig. 2.5):". First, it is unclear from the wording of this phrase as to whether it is intended to encompass both the list

of sequences set forth immediately after the phrase and any "other partial sequences of the alanine dehydrogenase gene of *M. tuberculosis*", or whether the list of sequences set forth constitutes all the "partial sequences and other partial sequences" encompassed by the phrase. Second, it is unclear as to how the recitation of "(Fig. 2.5)" is intended to limit the claim, as Figure 2.5 appears to set forth the same sequences recited in claim 1. Clarification is required with respect to what sequences are intended to be encompassed by the claim.

Claim 1 is indefinite over the recitation of the term "AlaDH-F2 5'-GAGACCAAAAC AACGAA-3'". The term "AlaDH-F2" is used in the specification to describe two different sequences (see claim 1 and page 4 of the specification as compared to Table 2.5 (page 14) and SEQ ID NO: 13). Accordingly, it is unclear as to whether the recitation in the instant claim is intended to encompass multiple sequences, or merely the sequence set forth to the right of the term "AlaDH-F2". Clarification is required.

Claim Rejections - 35 U.S.C. § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Katsumata et al (U.S. Patent No. 5,559,016 [9/1996]) in view of Ahern (The Scientist 9(15):20 [7/1995]).

The claim is drawn to a "set" that comprises an "enzymatic test kit" comprising L-alanine, NAD+, PMS, and NBT, and a "DNA sequence" selected from those "partial sequences" set forth in the claim and "other partial sequences of the alanine dehydrogenase gene of *M. tuberculosis*", as well as partial sequences thereof and sequences "that are hybridizable therewith". It is noted that the intended use of a product for which a clear and complete structural description is provided is not accorded patentable weight (see MPEP 2111.02).

Katsumata et al teach methods for producing alanine that employ cloned bacterial genes encoding L-alanine dehydrogenase (see entire reference, e.g., col 2, lines 26-36). It is a property of any of the genes taught by Katsumata et al that they would be "hybridizable with" any of the sequences set forth in claim 1, as any two sequences may be "hybridizable with" one another under conditions of sufficiently low stringency. Accordingly, Katsumata et al teach DNA sequences meeting the limitations set forth in the instant claim. Katsumata et al also disclose that clones encoding functional L-alanine dehydrogenase genes may be identified by employing a stain comprising NAD, L-alanine, PMS, and NBT (see Example, especially col 6, lines 46-49). Accordingly, Katsumata et al disclose a method in which all the components set forth in claim 1 are employed. However, Katsumata et al does not teach or suggest packaging NAD, L-alanine, PMS, and NBT into a kit, or suggest preparing a "set" comprising this kit and their DNA sequences. Ahern teaches that pre-made reagents provided in kit form are convenient and save researchers time and money (see p. 3/5-4/5). It is a property of any kit that it is a type of "set" comprising particular reagents packaged together. In view of the teachings of Ahern, it would

have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Katsumata et al so as to have packaged any or all of the reagents taught by Katsumata et al into a kit or "set". An ordinary artisan would have been motivated to have made such a modification in order to have provided the reagents needed to perform Katsumata et al's method for producing alanine to practitioners in a convenient format for the advantages of efficiency and cost-effectiveness.

12. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Andersen et al (Inf. Immun. 60(6):2317-2323 [6/1992]) in view of Ahern.

This rejection applies to the claim as it may be limited to a "set" comprising DNA sequences that comprise any of the particular sequences set forth in claim 1, which appear to correspond to instant SEQ ID Nos 11-25. Andersen et al teach the nucleotide sequence of the *M. tuberculosis* L-alanine dehydrogenase gene, which comprises each of the sequences set forth in instant SEQ ID Nos 11-25 (see Andersen et al, Figure 5). Andersen et al further teach that L-alanine dehydrogenase activity may be identified by employing a stain comprising NAD, L-alanine, PMS, and NBT (p. 2318). Accordingly, Andersen et al disclose methods for characterizing L-alanine dehydrogenase in which all the components set forth in claim 1 are employed. However, Andersen et al does not teach or suggest packaging NAD, L-alanine, PMS, and NBT into a kit, or suggest preparing a "set" comprising this kit and their DNA sequence. Ahern teaches that pre-made reagents provided in kit form are convenient and save researchers time and money (see p. 3/5-4/5). It is a property of any kit that it is a type of "set" comprising

particular reagents packaged together. In view of the teachings of Ahern, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Andersen et al so as to have packaged any or all of the reagents taught by Andersen et al into a kit or "set". An ordinary artisan would have been motivated to have made such a modification in order to have provided the reagents needed to perform Andersen et al's methods to practitioners in a convenient format for the advantages of efficiency and cost-effectiveness.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday from 7:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at 703/308-1152. The fax phone number for the Technology Center where this application or proceeding is assigned is 703/305-3014 or 305-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana Johannsen

July 10, 2000

Carla Myers

CARLA J. MYERS
PRIMARY EXAMINER

Application No.:09/362,485

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s)

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [X] 7. Other: Possible error in Sequence Listing; see attached Office action.

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE